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April 4, 2002

FILE: UTSD:857US

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Commissioner for Patents  
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RE: SN 10/076,918 "TRAF6-REGULATED IKK ACTIVATORS (TRIKA1 AND TRIKA2)  
AND THEIR USE AS ANTI-INFLAMMATORY TARGETS" - Zhijian J. Chen and Li  
Deng

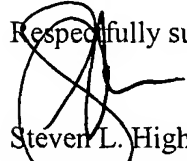
Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references (A1-A4, B1-B2, C1-C45).

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is hereby authorized to deduct said fees from Fulbright & Jaworski Deposit Account No.: 50-1212/10107423/SLH.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

  
Steven L. Highlander  
Reg. No. 37,642

SLH/cmb

Encl: as noted



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
Zhijian J. Chen  
Li Deng

Serial No.: 10/076,918

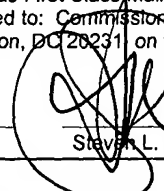
Filed: October 11, 2001

For: TRAF6-REGULATED IKK ACTIVATORS  
(TRIKA1 AND TRIKA2) AND THEIR  
USE AS ANTI-INFLAMMATORY  
TARGETS

Group Art Unit: Unknown

Examiner: Unknown

Atty. Dkt. No.: UTSD:857US/SLH

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Date	Steven L. Highlander

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
Washington, D.C. 20231

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

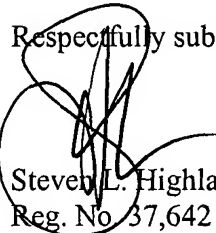
In accordance with 37 C.F.R §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be

an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R. § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is hereby authorized to deduct said fees from Fulbright & Jaworski Deposit Account No.: 50-1212/10107423/SLH.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,

  
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Attorney for Applicants

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Date: April 4, 2002

Form PTO-1449 (modified)	Atty. Docket No. UTSD:857US/SLH	Serial No. 10/076,918
List of Patents and Publications for Applicant's INFORMATION DISCLOSURE STATEMENT	Applicant Zhijian J. Chen Li Deng	
(Use several sheets if necessary)	Filing Date: October 11, 2001	Group: Unknown
U.S. Patent Documents See Page 1	Foreign Patent Documents See Page 1	Other Art See Page 1



### U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	5,708,142	1/13/98	Goeddel <i>et al.</i>	530	350	5/27/94
	A2	5,710,013	1/20/98	Goeddel <i>et al.</i>	435	29	4/19/96
	A3	5,741,667	4/21/98	Goeddel <i>et al.</i>	435	69.1	5/22/95
	A4	5,767,244	6/16/98	Goeddel <i>et al.</i>	530	350	11/20/97

### Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	B1	JP 00197500	7/18/00	Japan			Abstract
	B2	WO 99/40202	8/12/99	PCT			Abstract

### Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Ansieau <i>et al.</i> , "Tumor necrosis factor receptor-associated factor (TRAF)-1, TRAF-2, and TRAF-3 interact in vivo with the CD30 cytoplasmic domain; TRAF-2 mediates CD30-induced nuclear factor kappa B activation," <i>Proc. Nat'l Acad. Sci. USA</i> 93:14053-14058, 1996.
	C2	Cao <i>et al.</i> , "IRAK: a kinase associated with the interleukin-1 receptor," <i>Science</i> 271:1128-1131, 1996.
	C3	Cao <i>et al.</i> , "TRAF6 is a signal transducer for interleukin-1," <i>Nature</i> 383:443-446, 1996.
	C4	Chau <i>et al.</i> , "A multiubiquitin chain is confined to specific lysine in a targeted short-lived protein," <i>Science</i> 243:1576-1583, 1989.
	C5	Chen <i>et al.</i> , "Signal-induced site-specific phosphorylation targets I $\kappa$ B $\alpha$ to the ubiquitin-proteasome pathway," <i>Genes &amp; Dev.</i> , 9:1586-1597, 1995.
	C6	Chen <i>et al.</i> , "Site-specific phosphorylation of I $\kappa$ B $\alpha$ by a novel ubiquitination-dependent protein kinase activity," <i>Cell</i> 84:853-862, 1996.

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EXAMINER: INITIAL IF REFERENCE CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED. INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

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Exam. Init.	Ref. Des.	Citation
	C7	Cheng <i>et al.</i> "Involvement of CRAF1, a relative of TRAF, in CD40 signaling," <i>Science</i> , 267:1494-1498, 1995.
	C8	Courtois <i>et al.</i> , "Characterization of a mutant cell line that does not activate NF- $\kappa$ B in response to multiple stimuli," <i>Mol. Cell. Biol.</i> 17:1441-1449, 1997.
	C9	Davis, "Signal transduction by the JNK group of MAP kinases," <i>Cell</i> , 103:239-252, 2000.
	C10	Deng <i>et al.</i> "Activation of the I $\kappa$ B kinase complex by TRAF6 requires a dimeric ubiquitin-conjugating enzyme complex and a unique polyubiquitin chain," <i>Cell</i> , 103:351-361, 2000.
	C11	Dinareello, "Biologic basis for interleukin-1 in disease," <i>Blood</i> 87:2095-2147, 1996.
	C12	Farrar <i>et al.</i> , "Activation of the Raf-1 kinase cascade by coumermycin-induced dimerization," <i>Nature</i> , 383:178-181, 1996.
	C13	Finley, "An alternative to destruction," <i>Nature</i> , 412:283-286, 2001.
	C14	Gedrich <i>et al.</i> , "CD30 contains two binding sites with different specificities for members of the tumor necrosis factor receptor-associated factor family of signal transducing proteins," <i>J. Biol. Chem.</i> 271:12852-12858, 1996
	C15	Ghosh <i>et al.</i> , "NF- $\kappa$ B and REL proteins: evolutionarily conserved mediators of immune responses," <i>Annu. Rev. Immunol.</i> , 16:225-260, 1998.
	C16	Hatada <i>et al.</i> , "NF- $\kappa$ B and the innate immune response," <i>Curr Opin Immunol</i> , 12(1):52-58, 2000
	C17	Haung <i>et al.</i> , "Recruitment of IRAK to the interleukin 1 receptor complex requires interleukin 1 receptor accessory protein," <i>Proc Nat'l Acad Sci USA.</i> , 94(24):12829-12832, 1997.
	C18	Hershko and Heller, "Occurrence of a polyubiquitin structure in ubiquitin-protein conjugates," <i>Biochem. Biophys. Res. Commun.</i> , 128:1079-1086, 1985.
	C19	Hofmann and Pickart, "Noncanonical MMS2-encoded ubiquitin-conjugating enzyme functions in assembly of novel polyubiquitin chains for DNA repair," <i>Cell</i> , 96:645-653, 1999.
	C20	Hsu <i>et al.</i> , "TRADD-TRAF2 and TRADD-FADD interactions define two distinct TNF receptor 1 signal transduction pathways," <i>Cell</i> , 84:299-308, 1996.
	C21	Hu <i>et al.</i> , "A novel RING finger protein interacts with the Cytoplasmic domain of CD40," <i>J. Biol. Chem.</i> , 269:30069-30072, 1994.

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INFORMATION DISCLOSURE STATEMENT — PTO-1449 (MODIFIED)

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Exam. Init.	Ref. Des.	Citation
	C22	Ishida <i>et al.</i> "Identification of TRAF6, a novel tumor necrosis factor receptor-associated factor protein that mediates signaling from an amino-terminal domain of the CD40 cytoplasmic region," <i>J. Biol. Chem.</i> , 271:28745-28748, 1996.
	C23	Laney and Hochstrasser, "Substrate targeting in the ubiquitin system," <i>Cell</i> , 97:427-430, 1999.
	C24	Lee <i>et al.</i> , "Activation of the I $\kappa$ B $\alpha$ kinase complex by MEKK1, a kinase of the JNK pathway," <i>Cell</i> , 88:213-222, 1997.
	C25	Lee <i>et al.</i> , "MEKK1 activates both I $\kappa$ B kinase $\alpha$ and I $\kappa$ B kinase $\beta$ ," <i>Proc. Nat'l Acad. Sci. USA</i> , 95:9319-9324, 1998.
	C26	Lomaga <i>et al.</i> , "TRAF6 deficiency results in osteopetrosis and defective interleukin-1, CD40, and LPS signaling," <i>Genes Dev.</i> , 13:1015-1024, 1999.
	C27	Lorick <i>et al.</i> , "RING fingers mediate ubiquitin-conjugating enzyme (E2)-dependent ubiquitination," <i>Proc. Nat'l Acad. Sci. USA</i> , 96:11364-11369, 1999.
	C28	Mosialos <i>et al.</i> , "The Epstein-Barr virus transforming protein LMP1 engages signaling proteins for the tumor necrosis factor receptor family," <i>Cell</i> , 80:389-399, 1995.
	C29	Naito <i>et al.</i> , "Severe osteopetrosis, defective interleukin-1 signalling and lymph node organogenesis in TRAF6-deficient mice," <i>Genes to Cells</i> , 4:353-362, 1999.
	C30	Nakano <i>et al.</i> "TRAF5, an activator of NF- $\kappa$ B and putative signal transducer for the lymphotoxin- $\beta$ receptor," <i>J. Biol. Chem.</i> , 271:14661-14664, 1996.
	C31	Ninomiya-Tsuji <i>et al.</i> , "The kinase TAK1 can activate the NIK-I $\kappa$ B as well as the MAP kinase cascade in the IL-1 signalling pathway," <i>Nature</i> , 398:252-256, 1999.
	C32	Raingeaud <i>et al.</i> "MKK3- and MKK6-regulated gene expression is mediated by the p38 mitogen-activated protein kinase signal transduction pathway," <i>Mol. Cell. Biol.</i> , 16:1247-1255, 1996.
	C33	Régnier <i>et al.</i> , "Identification and characterization of an I $\kappa$ B kinase," <i>Cell</i> , 90:373-383, 1997.
	C34	Rothe <i>et al.</i> , "TRAF2-mediated activation of NF- $\kappa$ B by TNF receptor 2 and CD40," <i>Science</i> , 269:1424-1427 1995.
	C35	Rothofsky and Lin, "CROC-1 encodes a protein which mediates transcriptional activation of the human FOS promoter," <i>Gene</i> , 195:141-149, 1997.

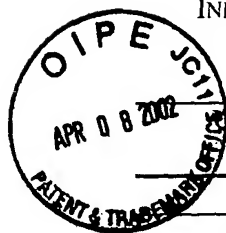
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Exam. Init.	Ref. Des.	Citation
✓	C36	Sancho <i>et al.</i> , "Role of UEV-1, an inactive variant of the E2 ubiquitin-conjugating enzymes, in in vitro differentiation and cell cycle behavior of HT-29-M6 intestinal mucosecretory cells," <i>Mol. Cell. Biol.</i> , 18:576-589, 1998.
✓	C37	Sato <i>et al.</i> , "A novel member of the TRAF family of putative signal transducing proteins binds to the cytosolic domain of CD40," <i>FEBS Lett.</i> , 358:113-118, 1995.
✓	C38	Simonsen and Stenmark, "PX domains: attracted by phosphoinositides," <i>Nature Cell Biol.</i> , 3:E179-E182, 2001.
✓	C39	Smith <i>et al.</i> , "The TNF receptor superfamily of cellular and viral proteins: activation, costimulation, and death," <i>Cell</i> , 76:959-962, 1994.
✓	C40	Song and Donner, "Association of a RING finger protein with the cytoplasmic domain of the human type-2 tumour necrosis factor receptor," <i>Biochem. J.</i> , 309:25-829, 1995.
✓	C41	Spencer <i>et al.</i> , "Signal-induced ubiquitination of IκBα by the F-box protein Slimb/β-TrCP," <i>Genes Dev.</i> , 13:284-294, 1999.
✓	C42	Takaesu <i>et al.</i> , "Interleukin-1 (IL-1) receptor-associated kinase leads to activation of TAK1 by inducing TAB2 translocation in the IL-1 signaling pathway," <i>Mol. Cell. Biol.</i> , 21(7):2475-2484, 2001.
✓	C43	Takaesu, <i>et al.</i> "TAB2, a novel adaptor protein, mediates activation of TAK1 MAPKKK by linking TAK1 to TRAF6 in the IL-1 signal transduction pathway," <i>Mol. Cell</i> , 5:649-658, 2000.
✓	C44	Wang <i>et al.</i> , "TAK1 is a ubiquitin-dependent kinase of MKK and IKK," <i>Nature</i> , 412:346-351, 2001.
✓	C45	Zapata <i>et al.</i> , "A diverse family of proteins containing tumor necrosis factor receptor-associated factor domains," <i>J. Biol. Chem.</i> , 276(26):24242-24252, 2001.

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